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Achalasia: Pre-operative tests, post-operative symptoms and surgical outcomes

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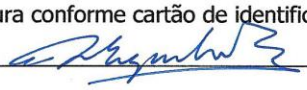

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Achalasia: Pre-operative tests, post-operative symptoms and surgical outcomes

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Dedicatória

Dedico esta tese aos meus pais, à Isabel Sousa, aos meus avós e a todos os familiares e amigos que me apoiaram de qualquer forma ao longo deste percurso na FMUP, em todo e qualquer momento. Sozinho seria uma tarefa muito mais difícil. Um profundo agradecimento a todos eles.

Title: Achalasia: Pre-operative tests, post-operative symptoms and surgical outcomes

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ABSTRACT

Purpose: The main goal of this study was to search for predictors, of post-operative dysphagia and heartburn, need for medical treatment during follow-up and the occurrence on intra and post-operative morbidity in patients with achalasia.

Methods: The records of the patients who underwent myotomy for achalasia from 2005 to 2014 were reviewed (n=46). Data regarding pre-operative and post-operative manometry and pH-metry was compiled, along with patients' symptoms and characteristics..

Results: Our sample was composed by 25 female patients and 21 male patients. No parameter of the conventional manometry was associated with post-operative dysphagia, heartburn or medical treatment. Pre-operative heartburn and regurgitation were associated with less post-operative dysphagia ($p<0.01$ and $p=0,034$, respectively); Pre-operative dilatations were associated with post-operative morbidity ($p=0.035$) but not with intra-operatory morbidity ($p=0.898$). Relapse of achalasia was associated with greater usage of PPI during follow-up ($p= 0.028$).

Conclusions: Heller myotomy is an effective treatment option for Achalasia. Dilatations should be used carefully since they can lead to an increase in post—operative morbidity. Patients with relapse of achalasia are more likely to need medical treatment after re-intervention while patients with pre-operative regurgitation and heartburn have less post-operative dysphagia.

INTRODUCTION

Achalasia is a disorder of oesophageal motility characterized by impaired relaxation of the lower oesophageal sphincter (LES), frequently associated with an increase in the pressure of LES and an absence of peristalsis of the oesophageal body [1]. Complete lower esophageal sphincter (LES) relaxation occurs in approximately 15–30% of patients with achalasia and is not a characteristic of early achalasia [2]. It's annual incidence is about 1 case per 100000 habitants and the prevalence is around 10 in 10000 [3]. There is no sexual and racial prevalence and, while it is a disease that can appear at any age, there are two peaks of incidence: between 20-40 years old and between 70-80 years old [3, 4].

The main symptom is dysphagia, usually progressive for solids and liquids, although it can also present itself as paradoxal dysphagia. Other common presentation symptoms include thoracic pain, regurgitation, heartburn and weight loss [1, 5].

As of now, the pathogenesis of this disease is unknown, [6] although it is hypothesized that it results from the loss of the ganglionic cells of the myenteric plexus of the esophagus [1]. Other current train of thought deals with a possible viral etiology [7, 8]. Achalasia has been associated with, at various degrees of risk, squamous cell carcinoma. However, there are no recommendations for screening for cancer in patients with Achalasia [3, 9].

Diagnosing Achalasia requires a high index of clinical suspicion. The current gold-standard is the oesophageal manometry [6]. A complete workup usually includes oesophageal manometry, upper gastrointestinal endoscopy and a barium esophagogram [3]. The cardinal feature of this disease is the impaired relaxation of the LES in response to swallowing. Other abnormalities include an increase in the LES pressure and absence of peristalsis in the oesophageal body [10]. Currently, there are two forms of manometry, conventional and the more recent high-resolution manometry (HRM). Conventional manometry has some disadvantages in comparison to HRM manometry, since it is unable to account for the intrabolus pressure, the crural diaphragm relaxation, radial asymmetry of the gastroesophageal junction (GEJ) and deglutive oesophageal shortening [11]. As for the upper gastrointestinal endoscopy, it's important to exclude a serious differential diagnosis, the Pseudo-Achalasia [6]. Barium esophagogram can also help in the diagnosis, identifying the so called "Bird's Beak [3, 6]. The advancements brought by HRM allowed the classification of Achalasia into 3 different subtypes, a classification known as the Chicago Classification of Motility Disorders [12]. Type I

represents classic achalasia, associated with low intra-oesophageal pressure and minimum levels of oesophageal contractility; Type II is characterized by panoesophageal pressure elevations and an absence of peristalsis [1]; Type III is usually called "spastic achalasia" [5, 10, 13]. HRM proved to be an important evolution in terms of diagnosis and classification of Achalasia [14, 15].

The available treatments are used for symptom relief. Currently, no curative interventions exist [1]. Regarding pharmaceutic interventions, the most common drugs used are calcium channel blockers, but they are ineffective [4, 16]. The other treatment options are injection of botulin toxin, pneumatic dilatation and surgery. Regarding botulin toxin injection, it's ineffective in the long term, with its' effects reverting in a period between 6 and 9 months after the intervention [5]. It is currently reserved for elderly patients and high surgical risk patients [4]. Pneumatic dilatation and surgical myotomy are more useful treatment options. Pneumatic dilatation is performed by insufflating a balloon in the distal oesophagus, causing the forced distension of the muscular fibers of the LES. Usually a balloon of 30 mm is used due to a lower perforation rate [17]. It's possible to achieve similar long-term results to surgery with pneumatic dilatation if multiple dilatations are used. It seems to be a more effective treatment in patients over 40 years old [16, 18]. It is also the most cost effective procedure [4] and has a lower risk of gastroesophageal reflux disease [17]. Surgery is the gold-standard treatment and the most frequently used surgical procedure is Heller's myotomy, performed laparoscopically (section of the muscular fibers of the LES). The laparoscopic approach results in shorter hospitalization times [19]. To prevent gastroesophageal reflux a partial fundoplicature must also be performed in conjunction with the myotomy [3, 16]. There seems to be no difference between the two different partial fundoplicatures, Dor or Toupet [20]. For the myotomy, most surgeons will perform a section of 6-8 cm of the LES fibres in the oesophagus and prolong it 1-2 cm into the stomach [21]. Surgery has great success rate in the long term [22], even though it is not completely free of complications and does not warrant the absence of relapse. Choosing between pneumatic dilatation or surgery has been a topic of recent discussion. A recent European RCT could not determine which approach was better, finding no statistical difference between them [17]. The symptom which shows greater improvement with surgery is regurgitation, in contrast with heartburn [20]. In general, post-surgical complications are scarce, with one studying relating incidence of complications in less than 4% of patients [23]. The most frequent adverse effect of the surgical intervention is gastroesophageal reflux. Another complication is the perforation of the oesophagus,

usually reported in around 5-10% of myotomies. A robotically assisted myotomy has been shown to lower the rate of perforation to 0% [24].

A new technique has been developed, known as POEM (per-oral endoscopy myotomy). In this technique the LES is sectioned through a tunnel created in the esophagus submucosa. [22]. The results using this technique have been promising, with significant decreases of the LES pressure [25]. One of the main criticisms of this approach is the lack of an anti-reflux procedure. In fact a study showed that around 46% patients had significative reflux just 6 months after the intervention [26].

The main goal of this study was to search for a relation between the parameters evaluated in the conventional manometry and the relapse of dysphagia post-operatively, the presence of post-operative heartburn and the usage of protein-pump inhibitors during follow-up. A secondary objective was to provide a report of the patients' symptoms (pre-op and post-op) and characteristics' and whether any of these factors could predict the development of post-operative dysphagia, heartburn and the usage of PPI drugs as well as the occurrence of intra-operative and post-operative morbidity.

METHODS

Subjects and study protocol: We performed a retrospective observational study of all patients, admitted in the Upper Gastrointestinal Unit of Centro Hospitalar de São João, who underwent surgery for Achalasia, be it primary or relapse, between 1st of January 2005 and 14th May 2014. The sample consisted of 46 patients, 25 female and 21 male. Patients younger than 18 years were excluded. To fulfil our aims, patient data was collected using the informatized systems of the hospital, and by consulting the manometry reports archived on paper. Patient data was compiled in an electronic database.

To evaluate the relation between manometric parameters and the post-operative symptoms, surgical complications, relapse of dysphagia and need for medical treatment, we reviewed all available manometric records, both pre-operatively and post-operatively. A sub-population of 20 patients, which had complete manometric data for both the pre-operative and post-operative periods, was created to evaluate the relation between pre-operative manometric parameters and post-operative outcomes. The variables used were: age at diagnosis; gender; diagnosis (primary achalasia or relapse); number of comorbidities; number of previous surgical procedures; pre-operative dilatations; type of surgery (heller-dor or totalization of myotomy); approach (laparoscopy or laparotomy); intra-operative morbidity; hospitalization length; post-operative morbidity; proton pump inhibitors (PPI) treatment during follow-up (starting in the first post-operative consultation or later) . Comorbidities were evaluated using Charlson Comorbidity Index [27] and morbidity was evaluated using the Clavien-Dindo Classification [28].

The symptoms recorded were: aspiration; siallorhea; halitosis; weight loss; chest Pain; bloating; heartburn; dysphagia; nocturnal cough; eructation; regurgitation; vomiting; nausea. Manometric variables evaluated were LES resting pressure; LES basal pressure; esophageal peristalsis; percentage of LES relaxation and LES functional length for both pre-operative and post-operative examinations.

Ambulatory 24-hour Esophageal pH Monitoring: This examination was performed using a pH Orion II® (single crystal antimony multi-use pH catheter) catheter equipped with 2 electrodes. Catheters were introduced through transnasal approach and the sensors were placed at 15 cm and 5 cm from the GEJ (pH channel 1 and 2 respectively), whose location had been previously determined by manometry. We instructed patients to perform their regular routines, and to record their meal times, the time of sleep and whenever they experienced symptoms. After an average of 24 hours, patients returned to the hospital

to remove the sensors and check the information recorded. Data analysis using MMS® software was performed, including the calculation of the DeMeester score.

Manometry: Patients were submitted to the test in the supine position, after a fasting period of 12 hours. The test was performed using a manometric tube with 8 sensors, 4 placed in the distal end and 4 along the tube, 5 cm apart. This tube was inserted transnasally until the EGJ and then removed, cm by cm, by stationary pull-through so as to measure LES basal (normal: 10-25 mmHg) and residual pressures. LES relaxation was analysed using wet swallows of water (5mL). Relaxation was considered complete when LES pressure decreased to levels of gastric baseline pressure. Peristalsis was evaluated with a series of ten wet swallows.

Surgical Procedure: The surgery was performed either by laparoscopy or laparotomy. The patient was placed in a modified lithotomy position. In the laparoscopic procedure the procedure began with the creation of a pneumoperitoneum. Afterwards five trocars were inserted. The liver was retracted. After the opening of the crura, the oesophagus was dissected into the mediastinum. Next the short gastric vessels were mobilized so as to facilitate the partial fundoplicature. The EGJ was identified and the myotomy was then performed using an L-shaped hook electrocautery device or an UltraCision ® device, cutting the longitudinal muscle fibers first. The circular muscle fibers were then exposed and sectioned. The myotomy was performed with a length of 6-8 cm in the esophagus and prolonged distally 1-2 cm to the stomach. After finishing the myotomy, a Dor fundoplicature was performed. As for the laparotomy approach, the procedure was similar, except that it was performed with a supraumbilical median incision.

Statistical analysis: Statistical analysis was performed using IBM SPSS22 Statistics ®. Student t test was used to analyse independent samples when comparing two groups and the variables were quantitative. To assert whether a variable had a normal distribution or not, the Levene and the Kolmogorov-Smirnov tests were used. If normality could not be asserted, the proper non-parametric test (Mann-Whitney test) was used. When studying categorical variables, crosstabs were created and $\chi 2$-test or Fisher's exact test were applied, according to the situation. To evaluate whether pre-operative factors affected the risk of post-operative outcomes, we performed logistic regression. Tests results were considered statistical significant for a level of $p<0.05$.

RESULTS

A total of 46 patients were operated in our centre from 2005 to 2014. Mean age at diagnosis was 48.02 ± 17.79 years old (range: 18-81 years old). 45.7% of patients were male and 54.3% were female. 40 patients had been diagnosed for the first time with Achalasia and 6 patients had relapse of the disease. Male patients had a lower age at diagnosis (46.10 years) when compared to female patients (49.64 years) without statistical difference (p=0.516).

In our sample, 52.2% of patients had no comorbidities, 10.9% had 1, 17.4% had 2 comorbidities and 19.6 had more than 2. Applying the Charlson Comorbidity Index, 4 patients had grade I complications, 3 had grade II, 2 had grade III and only one had grade IV comorbidities. It's also important to point out that one patient had multiple sclerosis and another had Down syndrome.

The majority of the patients in our study had no prior surgical procedures (76.1%); 17.4% had 1; 4.3% had 2 surgical procedures and only 2.2% had been subjected to 3 surgeries before.

In terms of pneumatic dilatations, 14 patients (30. 4%) had dilatations prior to surgery. No information was found regarding the specific number of dilatations of 2 patients. Mean number of dilatations was 2.25 ± 1.288.

In terms of the surgical technique used, 4 patients underwent myotomy totalization and the remaining patients were subjected to Heller-Dor surgery. No Toupet fundoplicature was performed. A cholecystectomy was performed in one patient in the same operative time, while 3 others underwent hiatal hernia correction in the same operative period.

Most operations were performed laparoscopically, with only 10.9% of interventions performed through laparotomy. Only one patient was previously operated using the POEM technique. This patient relapsed and was operated laparoscopically, having complaints of heartburn and light dysphagia for solids after the surgery but no need for PPI treatment.

The mean hospitalisation length was 6.10 days ± 10.67; the minimal period of stay was 2 days, while the maximum was 76 days (patient with Down syndrome, which developed nosocomial pneumonia and respiratory insufficiency).

A complete report on all the patients' symptoms and complaints pre-operatively and post-operatively, can be seen in table 1.Virtually all patients in the pre-operative period had dysphagia. Information regarding the type of dysphagia was difficult to collect using the medical reports, with information about 22 patients missing. Despite that, the data available showed that 2.2% had dysphagia just for liquids, 8.7% had

isolated dysphagia for solids, 1 patient (2.2%) had paradoxal dysphagia and 18 patients had dysphagia for liquids and solids. In our sample, 21.8% of patients had dysphagia post-operatively. 5 patients had dysphagia for solids, 4 had dysphagia for liquids and solids and 1 had dysphagia for liquids only.

No statistically significant associations were found between post-operative heartburn and pre-operative symptoms or patients' characteristics (Table 2).

A total of 23 patients performed a 24-hour pH-metry after the surgery. In our sample, 17.4% of patients had acid pathological reflux detected in the examination. Reflux was only detected in channel pH2, which was located at 5 cm from the GEJ. 75% of the patients who performed the examination showed no symptoms. 12.5% of patients had a negative symptom index while the remaining 12.5% had a positive symptom index. The association between post-operative complaints of heartburn and post-operative reflux demonstrated in 24-hour pH-metry was non-significant (p=0.281).

No associations were found between pre-operative data and post-operative dysphagia, except for pre-operative regurgitation and pre-operative heartburn (Table 2). Women had more dysphagia post-operatively (40% vs 37.5) but there was no statistical difference (p=0.538).

Patients who had pre-operative complaints of heartburn were less likely to have dysphagia post-operatively (25% vs 75%, p<0.01). Pre-operative heartburn and age at diagnosis were not associated (p=0.254). Patients that had pre-operative regurgitation had less dysphagia when compared with patients who did not have regurgitation prior to the surgery (13.2% vs 45.2% respectively, p=0.034). In our study, patients who had pre-operative regurgitation had a higher age at diagnosis (56.53 vs 43.90; p= 0.024).

The number of pre-operative co-morbidities was higher in patients with post-operative dysphagia (1.63 vs 0.86) but this difference was not significant (p=0.074). Patients who had post-operative dysphagia also had a higher age at diagnosis (50.94 vs 46.47 years old) but it wasn't statistically significant (p=0334).

In our population, 39.1% of patients started therapy with proton-pump inhibitors during follow-up. There were no differences between the patients who needed PPI treatment and those who didn't when it comes to the number of comorbidities (p=0.449), age (p=0.350), the number of surgical procedures (p=0.683) and the number of dilatations (p=0.148). There was an association between the type of diagnosis (primary achalasia or relapse) and the need for PPI treatment in the post-operative period (32.5% vs 83.3% respectively, p= 0.028).

No other statistically significant associations regarding post-operative PPI treatment were found (Table 2).

There was no association between the patients who had pre-operative dilatations and post-operative heartburn (p=0.189), post-operative dysphagia (p=0.739), need for medical treatment (p=0.332) or reflux in the post-operative pH-metry (p= 0.273).

The rate of intra-operative complications was 13%. Iatrogenic perforation of the oesophagus happened in 4 patients, and 2 other had intra-operatory aspiration of vomit. One of these patients also suffered a spleen laceration. Regarding post-operative morbidity, 8.7% of patients had complications. Surgical wound dehiscence (Grade I of the Clavien-Dindo classification) was present in one patient, while another had surgical wound infection (Grade II). One patient experienced left superior member palsy (Grade I) and finally one had nosocomial pneumonia (Grade IV). There was no mortality in our sample, except for the patient with Down syndrome, who died due to complications of the disease.

Concerning intra-operative morbidity, no predictors were found (Table 3). As for post-operative morbidity, patients who had a higher number of pre-operative dilatations had more morbidity after the surgery (p=0.035).

We compared the manometric profile of patients before and after the surgery (Table 4). A significant decrease of LES basal and residual pressures was verified. Average LES functional length was 3.4 cm ±1 cm. Before the surgery, 17 patients had positive intraoesophageal pressure and 7 had negative pressure. Post-operatively, only one patient had positive intraoesophageal pressure, while the remaining 24 had negative intraeosophageal resting pressure. The pre-operative and post-operatives manometric profiles did not differ with gender.

We performed logistic regression to see if any pre-operative aspect of the patients' manometric profile could have an impact in post-operative dysphagia, post-operative heartburn and the need for medical treatment. There were no statistically significant differences (Table 5).

DISCUSSION

Achalasia has no curative treatment. All available treatments are palliative and have the main purpose of assuring the passage of liquids and solids through the gastroesophageal junction, therefore alleviating the symptomatology, preventing food stasis in the oesophagus and ultimately allowing the patient to eat. Furthermore, our knowledge of the disease, in pathophysiological terms, is still suboptimal. This leads to difficulty in identifying predictors of favourable outcomes for all treatments, including surgery.

There have been previous reports regarding predictors of surgical success. One study reported that patients with a higher pre-operative score of dysphagia had better surgical outcomes [23], while other reported that a duration of symptoms longer than 10 years predicted more post-operative dysphagia [29]. This was also supported by Krishnamohan P et al., whose study also found that a sigmoid oesophagus shape in pre-operative tests was also a predictor of surgical success [30].

In this study we provide a complete report of the patients' complaints, both pre-operatively and post-operatively. The most commons symptoms before surgery, besides dysphagia, were heartburn and regurgitation. Heartburn remained the most common symptom even after surgery (34.8%). This is probably due to the fact that pre-operative and post-operative heartburn have different pathophysiological origins. This rate of heartburn is similar to other reports in the literature [31]. Despite this, only 17.4% of patients had had acid pathological reflux detected in the pH-metry post-operatively. This is in accordance to previous literature results [32] and can be explained by the low correlation between a patient complaining of heartburn and reflux and the demonstration of said reflux in the pH-metry.

One of our main goals was to try and find which pre-operative characteristics could predict better outcomes after the surgery, namely less dysphagia, less reflux, less intra-operative and post-operative complications and a lower usage of PPI medication.

Regarding post-operative dysphagia, we found two associations. First, patients which had pre-operative regurgitation had less post-operative dysphagia when compared with patients who did not have pre-operative regurgitation (13.3% vs 45.2%, respectively, p=0.034). Interestingly, patients with pre-operative regurgitation were older, at the time of diagnosis, than patients without regurgitation (56.53 vs 43.90; p= 0.024). This was the only symptom which showed an association with age. It is a well-known fact that older patients, particularly over 60, have better outcomes after surgery, including less post-operative dysphagia [33]. As such, we think that this predictor effect of regurgitation of a better outcome was due to the fact that, in our sample, patients who complained of said symptom were older. Secondly,

another interesting finding was that patients who had pre-operative complaints of heartburn were less likely to have dysphagia post-operatively ($p<0.01$). As in the case of regurgitation, patients who experienced pre-operative heartburn were older than patients who didn't (51.04 years old vs 44.10 years old), even though it was not statistically significant ($p=0.254$). It's possible that the explanation for this association is the same that we propose for the regurgitation and dysphagia association, and that our sample simply did not have the statistical power to demonstrate it.

The type of diagnosis, the type of surgical approach, the number of co-morbidities did not prove to be predictors of post-operative dysphagia. Although women had more dysphagia post-operatively (40% vs 37.5%) there was no significance ($p=0.538$). Contrary to what has been reported about the patient's age as a predictor of surgical outcomes [31], no association was found in our sample, even though patients who had post-operative dysphagia also had a higher age at diagnosis (50.94 vs 46.47 years old; $p= 0.334$).

In terms of heartburn, we did not find any factors that could predict a higher incidence of this symptom post-operatively. This seems to be the case with other similar studies [29]. 39.1% of our patients started proton-pump inhibitor medication during follow-up. Although we could not find any predictors for post-op heartburn, we did discover that the diagnosis can predict the need for PPI medication. Patients who had relapse of Achalasia were more likely to need PPI treatment (83.3% of patients with relapse needed PPI vs only 32.5% of patients with primary Achalasia; $p= 0.028$). No similar reports were found in the literature. A possible explanation may result from the fact that patients who relapse must endure a second myotomy, which further weakens the physiological anti-reflux mechanism, predisposing to more severe heartburn and a greater need for medication.

LHM plus Dor fundoplicature proved to be an excellent treatment option for Achalasia. Our rate of post-operative dysphagia rounded 21.8%, which is in accordance to the rates reported in the literature [4]. After the surgery there was a significant decrease in LES basal pressure (26.76 vs 6.41; $p<0.01$), as well as LES Residual pressure (13.10 vs 2,70, $p<0.01$). LES relaxation increased after the surgery (from 55.54% to 67,54%) even though this was not a statistically significant increase ($p=0.134$). Other studies have showed a non-significant increase as well [32].

As for the pre-operative manometric parameters, we did not find any association between these characteristics and post-operative dysphagia, need for medical treatment and post-operative heartburn (Table 4).

We also evaluated intra-operative and post-operative morbidity. Our rate of complications, 13% and 7%, respectively, is within the normal range reported in previous works [23, 30, 31].

When trying to assert possible predictors of morbidity, we found no factors that could predict intra-operative morbidity. However, we did find an association between pre-operative pneumatic dilatations and post-operative morbidity ($p=0.035$). Dilatations are one of the most effective treatments available for Achalasia [4]. Nonetheless, one must take into account that previous dilatations can make the surgical technique more challenging and can perhaps lead to more complications for patients. Multiple reports in the literature have associated the existence of previous treatments and poorer surgical outcomes, this effect being greater with botulin toxin injection [5, 34, 35]. Smith et al. state that, in patients with previous dilatations, the submucosal dissection plane is obliterated [36]. Nevertheless, other articles found no association between pre-operative dilatations and surgical outcomes [29, 31].

Taking this information into consideration, we think that pneumatic dilatations should be used carefully and that there should be a strict decision-making process on which patient does dilatation before surgery.

One recent development that might help in this decision is the Chicago Classification, since it has been shown that patients with type II achalasia as defined by this classification respond better to any form of treatment and this subtype is a predictor of therapeutical success [10]. On the other hand, type I and type III of the Chicago Classification tend to predict a poorer outcome [5].

The limitations of this study are the retrospective approach and the small sample size. Due to our sample size, a risk for a Type II error exists. Another limitation was the lack of complete data regarding the manometric reports of all patients.

In conclusion, our study reinforces the efficacy of LHM as the current gold-standard of treatment for Achalasia while introducing the notion that there should be an extra care in terms of reflux for patients with relapse of the disease. It also shows that pneumatic dilatations, while curiously a safe option in terms of intra-operative morbidity, can lead to a higher incidence of post-operative morbidity and, as such, should be used with great care. It is our opinion that prospective studies with long follow-up are needed to uncover new predictors of surgery success or failure, specially taking into account the differences between subtypes of Achalasia elucidated by the new Chicago Classification.

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ANNEXES

ANNEX I- Tables

Symptom	Pre-Operative Period		Post-Operative Period	
	Absolute Frequency	Relative Frequency	Absolute Frequency	Relative Frequency
Nausea	1	2,2%	5	10,9%
Vomit	4	8,7%	5	10,9%
Bloating/Fullness	2	4,3%	5	10.9%
Regurgitation	15	32,6%	6	13%
Heartburn	26	56,5%	16	34,8%
Chest Pain	8	17,4%	1	2,2%
Nocturnal Cough	3	6,5%	1	2,2%
Aspiration	1	2,2%	0	0
Sialorrhea	1	2,2%	1	2,2%
Halitosis	2	4,3%	1	2,2%
Weight Loss	9	19,6%	0	0
Eructation	2	4,3%	1	2,2%

Table 1: Patients's symptons, pre-operative and post-operative

Pre-operative symptoms/Patient data	N (%)	Post-op Dysphagia	Post-Op Heartburn	Post-Op PPI Treatment
Chest Pain	8 (17.4%)	p=1	p=1	p=1
Regurgitation	15 (32.6%)	p=0,878	p=0,034	p=0,503
Weight loss	9 (19.6%)	p=1	p=0,7	p=1
Nocturnal cough	3 (6.5%)	p=0,542	p=1	p=0,270
Heartburn	26 (56.5%)	p=0,433	p<001	p=0,805
Diagnosis (Primary or Relapse)		p=0,405	p=0,405	p=0,028
Primary Achalasia	40 (87%)			
Relapse	6 (13%)			
Surgical approach		p=1	p=0,602	p=0,284
Laparoscopic	41 (89.1%)			
Laparotomy	5 (10.9%)			
Intra-Operative Morbidity	6 (13%)	p=0,405	p=0,649	p=1

Table 2: Associations between patient data and post-operative dysphagia, heartburn and PPI treatment

Patient Data	Mean	Intra-Operative Morbidity (p value)	Post-Operative Morbidity (p value)
Age	48.02	0.794	0.575
Number of dilatations	0.61	0.898	0.035
Number of surgeries	0.33	0.778	0,781
Number of comorbidities	1.11	0.997	0,281

Table 3: Predictors of intra-operative and post-operative morbidity

Manometric Parameters	Pre-Operative		Post-Operative		P value
	Mean	Standard Deviation	Mean	Standard Deviation	
LES basal pressure	26,76	13,179	6,41	2,785	<0.01
LES residual pressure	13,10	5,174	2,70	2,163	0,001
LES relaxation (%)	55,54	13,617	67,54	20,602	0,134

Table 4: Differences between manometric profiles, before and after surgery (LES: Lower esophageal sphincter)

Pre-operative Manometric parameters	Post-operative Heartburn (p value)	Post-Operative Dysphagia (p value)	PPI Treatment (p value)
LES basal pressure	0.906	0.421	0.395
LES residual pressure	0.728	0.233	0.265
LES relaxation pressure	0.866	0.471	0.387
LES functional length	0.326	0.358	0.851

Table 5: Manometric profile and the association with post-operative heartburn, dysphagia and PPI treatment (LES: Lower esophageal sphincter)

ANNEX 2 – *Surgery Today* magazine rules

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Spreadsheets:

Spreadsheets should be converted to PDF if no interaction with the data is intended.
If the readers should be encouraged to make their own calculations, spreadsheets should be submitted as .xls files (MS Excel).

Collecting Multiple Files:

It is possible to collect multiple files in a .zip or .gz file.

Accessibility:

In order to give people of all abilities and disabilities access to the content of your supplementary files, please make sure that the manuscript contains a descriptive caption for each supplementary material
Video files do not contain anything that flashes more than three times per second (so that users prone to seizures caused by such effects are not put at risk)
(Revised on January 20, 2015)

ANNEX 3- Ethics committee approval

Direcção Clínica CES 155-14
30 12 2014

AUTORIZADO
08 JAN 2015

Exmo. Senhor
Presidente do Conselho de Administração do
Centro Hospitalar de S. João – EPE

Assunto: Pedido de autorização para realização de estudo/projecto de investigação

Nome do Investigador Principal: Raul Miguel de Freitas Lima Neto (Aluno de Mestrado Integrado em Medicina – FMUP)

Título do projecto de investigação: Acalásia: Correlação entre achados manométricos e endoscópicos pré-operatórios e a presença de complicações cirúrgicas e recorrência de sintomas

Pretendendo realizar no(s) Serviço(s) de Cirurgia Geral
do Centro Hospitalar de S. João – EPE o estudo/projecto de investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efectivação.
Para o efeito, anexa toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar de S. João respeitante a estudos/projectos de investigação, à qual endereçou pedido de apreciação e parecer.

Com os melhores cumprimentos.

Porto, 23 / Junho / 2014

O INVESTIGADOR/PROMOTOR

Comissão de Ética para a Saúde do Centro Hospitalar de S. João – EPE

Modelo CES 01

Comissão de Ética para a Saúde – Centro Hospitalar São João / FMUP

Parecer

Título do Projecto: Acalasia: correlação entre achados manométricos e endoscópicos pré-operatórios e a presença de complicações cirúrgicas e recorrência de sintomas.

Nome do Investigador Principal: Raul Miguel de Freitas Lima Neto

Local onde sera realizado o estudo: Serviço de Cirurgia Geral – CHSJ, havendo autorização do respectivo Diretor de Serviço para a realização do mesmo. *Falta designação do Elo de Ligação, bem como a respectiva Declaração.*

Objectivo do estudo: Comparar achados pré-operatórios com a recidiva de sintomas no pós-operatório de forma a tentar identificar possíveis achados que permitam prever a resposta do doente a dado tratamento.

Período previsto de conclusão: Dezembro 2014

Benefício / Risco: N/A

Respeito pela liberdade e autonomia do sujeito do ensaio: N/A

Confidencialidade dos dados: está garantida a confidencialidade dos dados e esta informação será restrita aos investigadores.

O Investigador Principal dispõe de competência técnica e científica para a realização do estudo.

Não prevê a realização de questionário.

Custos: O estudo não prevê custos acrescidos para a instituição.

Parecer: Em face da análise do protocolo de estudo, proponho a sua aprovação pela CES do CHSJ, após resposta à questão em itálico.

Porto, CHSJ, 15 de julho de 2014

O Relator

Dr. John Preto

7. SEGURO

a. *Este estudo/projecto de investigação prevê intervenção clínica que implique a existência de um seguro para os participantes?*

SIM ☐ (Se sim, junte, por favor, cópia da Apólice de Seguro respectiva)
NÃO ☐
NÃO APLICÁVEL ☑

8. TERMO DE RESPONSABILIDADE

Eu, Raul Miguel de Freitas Lima Neto,
abaixo-assinado, na qualidade de Investigador Principal, declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (com as emendas de Tóquio 1975, Veneza 1983, Hong-Kong 1989, Somerset West 1996 e Edimburgo 2000) e da Organização Mundial da Saúde, no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CES de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo no decurso do actual internamento ou da mesma consulta.

Porto, 23 / Junho / ~~20 14~~

A Comissão de Ética para a Saúde tendo aprovado o parecer do Relator, aguarda que o Investigador/Promotor esclareça as questões nele enunciadas para que possa emitir parecer definitivo.

O Investigador Principal

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética
2014.07.25

PARECER DA COMISSÃO DE ÉTICA PARA A SAÚDE DO CENTRO HOSPITALAR DE S. JOÃO

emitido na reunião plenária da CES de ___/___/___

Considerando que foram cumpridas as disposições e esclarecimentos prestados pelo investigador

A Comissão de Ética para a Saúde APROVA por unanimidade o parecer do Relator, pelo que nada tem a opor à realização deste projecto de investigação.

2014.08.18

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética